

One-carbon homologation of aryl and alkyl aldehydes to amides using $\text{BtCH}_2\text{P}^+\text{Ph}_3\text{Cl}^-$

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Dedicated to Professor Chengye Yuan on his 80th anniversary
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Abstract

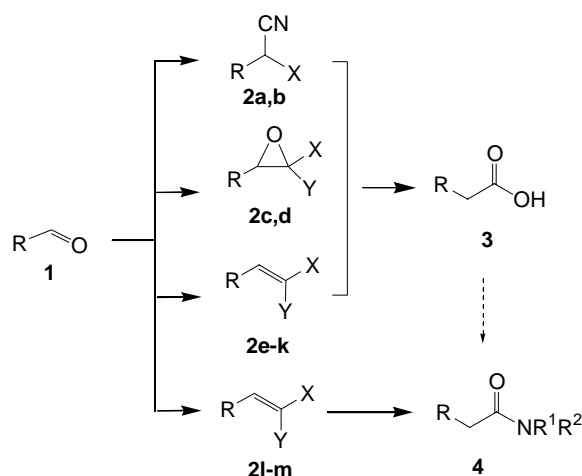
One-carbon homologated amides have been prepared from aryl and alkyl aldehydes. Vinyl benzotriazoles **6**, prepared by the reaction of aldehydes with the one-carbon synthon $\text{BtCH}_2\text{P}^+\text{Ph}_3\text{Cl}^-$ (**5**), were subsequently brominated to give 1,2-dibromo-benzotriazolylalkanes **7**. Treatment of **7** with a variety of aryl or alkyl amines in the presence of water furnished one-carbon homologated amides **8ar** in 32–95% yields. This method works well with both primary and secondary aryl or alkyl amines.

Keywords: Vinyl benzotriazole, 1,2-dibromo-benzotriazolylalkanes, homologation

Introduction

Previous methods for the one-carbon homologation of aldehydes to amides have mostly involved the one-carbon homologation of aldehydes **1** to carboxylic acids **3** followed by a functional group transformation to amides **4** (Scheme 1). Classical intermediates developed for the preparation of one-carbon homologated carboxylic acids **3** as summarized by Watt *et al.* include: cyanohydrins **2a**, nitriles **2b**, glycidic esters **2c**, epoxides **2d**, enol ethers **2e**, thioenol ethers **2f**, enamines **2g**, ketene thioacetals **2h**, α,β -unsaturated sulfones **2i**, or α,β -unsaturated phosphonates **2j** (Scheme 1).¹ Syntheses of intermediates **2a-j** and subsequent conversion to carboxylic acids **3** often require harsh conditions that are incompatible with sensitive functional groups. Reports of low yields using these intermediates and lack of sufficient examples indicate a limited scope. A one-pot procedure *via* 1-(benzotriazol-1-yl)-1-methoxyalk-1-enes **2k** for the preparation of homologated carboxylic acids from aldehydes has been reported (Scheme 1).² Amine solvolysis of α -alkoxyacrylonitriles **2l** gives one-carbon homologated amides directly but is inapplicable to substrates with acid-labile groups (Scheme 1).^{1a} The recently reported one-

carbon homologation of aldehydes to amides using 1,1-dibromo-1-alkenes **2m** offers a short route, good yields and mild reaction conditions that tolerate a range of functionalities but it is inapplicable to alkyl aldehydes and aryl amines and uses carcinogenic carbon tetrabromide (Scheme 1).^{3,4}



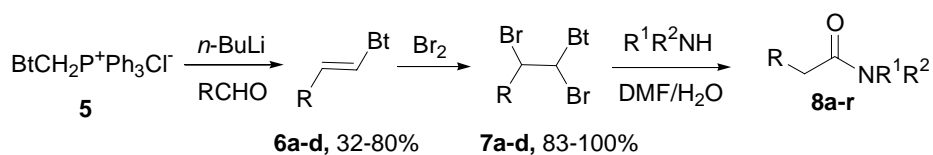
(**2a**) X = OH; (**2b**) X = H; (**2c**) X = H, Y = COOR; (**2d**) X = Y = H; (**2e**) X = H, Y = OMe, OPh;
 (**2f**) X = H, Y = SPh; (**2g**) X = N(CH₂)₄, NMe₂; (**2h**) X, Y = SMe, SPh, S(CH₂)₃S; (**2i**) X = SO₂Ph,
 Y = NHCHO; (**2j**) X = PO(OEt)₂, Y = NMe₂; (**2k**) X = Bt, Y = OMe; (**2l**) X = CN, Y = OAc;
 (**2m**) X = Y = Br

Scheme 1

Herein, we report a general method for the conversion of aldehydes to one-carbon homologated amides. Vinyl benzotriazoles **6** prepared from BtCH₂P⁺Ph₃Cl⁻ (**5**) and aldehydes⁵ were brominated to give 1,2-dibromo-benzotriazolylalkanes **7**. Subsequent treatment of **7** with a variety of aryl or alkyl amines in the presence of water furnished the desired one-carbon homologated amides **8a-r** in 32-95% yields. Our method is applicable to aryl and alkyl aldehydes as well as to primary and secondary aryl or alkyl amines and avoids the use of carbon tetrabromide.

Results and Discussion

Preparation of vinyl benzotriazoles and 1,2-dibromo-benzotriazolylalkanes. Reaction of BtCH₂P⁺Ph₃Cl⁻ (**5**) with *n*-BuLi and aryl or alkyl aldehydes (RCHO, R = Ph, 2-thienyl, *i*-Pr, Et) gave vinyl benzotriazoles **6a-d** in 32-80% yields following a previously reported general procedure (Scheme 2).⁵ Treatment of vinyl benzotriazoles **6 a-d** with bromine at 0 °C gave the corresponding 1,2-dibromo-benzotriazolylalkanes **7 a-d** in 83-100% yields (Scheme 2). Most of the dibromoalkanes were obtained in quantitative yields and could be used directly in the next step without further purification.



Scheme 2

Preparation of amides. Reaction of 1,2-dibromo-benzotriazolylalkanes **7 a-d** with various alkyl or aryl amines (5 equiv) in DMF/H₂O (3:1) furnished the desired amides **8 a-r** in 32-95% yields (Scheme 2, Table 1). The amides **8 a-r** were fully characterized by ¹H and ¹³C NMR spectroscopy, melting point and elemental analysis for novel compounds.

Table 1. Preparation of one-carbon homologated amides **8 a-r**

Entry	R	R ¹	R ²	Yield (%)
1	Ph	Ph(CH ₂) ₂	H	8a (47)
2	Ph	Bu	H	8b (58)
3	Ph	(CH ₂) ₅	–	8c (61)
4	Ph	Ph	H	8d (72)
5	Ph	<i>t</i> -Bu	H	8e (68)
6	Ph	2-pyridyl	H	8f (85)
7	Ph	1-pyrimidyl	H	8g (80)
8	2-thienyl	Ph(CH ₂) ₂	H	8h (52)
9	2-thienyl	Bu	H	8i (92)
10	2-thienyl	(CH ₂) ₅	–	8j (88)
11	<i>i</i> -Pr	(CH ₂) ₅	–	8k (50)
12	Et	Bu	H	8l (84)
13	Et	(CH ₂) ₂ N(CH ₃) ₂	H	8m (32)
14	Et	(CH ₂) ₂ O(CH ₂) ₂	–	8n (54)
15	Et	(CH ₂) ₂ N(CH ₃)(CH ₂) ₂	–	8o (62)
16	Et	Ph	H	8p (95)
17	Et	4-pyridyl	H	8q (82)
18	Et	α-naphthyl	H	8r (68)

The reaction of dibromoalkanes **7 a-d** with amines in DMF/H₂O is similar to the recently reported method by Shen and Kunzer involving the reaction of dibromoalkenes (prepared from aryl aldehydes) with alkyl amines.³ The use of benzotriazolyl intermediates **7 a-d** extends the applicability of this method and allows the preparation of one-carbon homologated amides from aryl or alkyl aldehydes and amines.

Conclusions

In summary, we have developed a general method for the preparation of one-carbon homologated amides from aldehydes *via* easily accessible 1,2-dibromo-benzotriazolylalkanes.

Experimental Section

General Procedures. Melting points were determined on a MEL-TEMP capillary melting point apparatus equipped with a Flucke 51 digital thermometer. ¹H NMR (300 MHz) and ¹³C NMR (75 MHz) spectra were recorded on a Gemini 300 NMR spectrometer in CDCl₃ (with TMS for ¹H and chloroform-*d* for ¹³C as the internal reference). Elemental analyses were performed on a Carlo Erba-1106 instrument. THF was distilled from sodium/benzophenone prior to use. All of the reactions with air sensitive compounds were carried out under N₂. Column chromatography was performed on silica gel 200–425 mesh.

Procedure for the preparation of benzotriazolyl alkenes **6a-d**

To a solution of 1-(1*H*-1,2,3-benzotriazolyl)-1-triphenyl methane chloride (21.7 g, 0.05 mol) in DMSO, *n*-BuLi (1.6 M, 31 mL, 0.05 mol) was added under nitrogen at 25 °C. One hour later aldehyde (0.06 mol) was added dropwise. After stirring for 12 h, the mixture was poured into water (150 mL), followed by extraction with CHCl₃ (4×50 mL). The combined extracts were washed with brine and dried over anhydrous MgSO₄. After removing the solvent *in vacuo*, the crude product was purified by column chromatography with hexanes/ethyl acetate (10:1) as eluent.

1-[(*E*)-2-Phenylethenyl]-1*H*-1,2,3-benzotriazole (6a**).** White microcrystals; mp 115–116 °C (Lit⁵ mp 115–117 °C); yield, 50%. ¹H NMR δ 7.28–7.62 (m, 8H), 7.74 (d, *J* = 8.3 Hz, 1H), 7.92 (d, *J* = 14.6 Hz, 1H), 8.09 (d, *J* = 8.3 Hz, 1H). ¹³C NMR δ 110.0, 120.4, 121.0, 121.7, 124.6, 126.5, 128.2, 128.4, 128.9, 131.4, 134.3, 146.3.

1-[(*E*)-2-(3-Thienyl)ethenyl]-1*H*-1,2,3-benzotriazole (6b**).** Yellow powder; mp 80–82 °C; yield, 68%. ¹H NMR δ 7.04 (dd, *J* = 3.3, 5.0 Hz, 1H), 7.17 (d, *J* = 3.3 Hz, 1H), 7.27 (d, *J* = 5.0 Hz, 1H), 7.41 (t, *J* = 7.7 Hz, 1H), 7.56 (t, *J* = 7.8 Hz, 1H), 7.60 (d, *J* = 14.4 Hz, 1H), 7.71 (d, *J* = 8.2 Hz, 1H), 7.78 (d, *J* = 14.4 Hz, 1H), 8.08 (d, *J* = 8.2 Hz, 1H). ¹³C NMR δ 109.8, 114.8,

120.3, 120.5, 124.6, 125.2, 127.5, 127.8, 128.2, 131.3, 138.2, 146.1. Anal. Calcd for C₁₂H₉N₃S: C, 63.41; H, 3.99; N, 18.49. Found: C, 63.65; H, 3.87; N, 17.89.

1-[(E)-3-Methyl-1-butenyl]-1H-1,2,3-benzotriazole (6c). Colorless oil; yield, 60%. ¹H NMR δ 1.21 (d, *J* = 6.9 Hz, 6H), 2.60–2.65 (m, 1H), 6.51 (dd, *J* = 14.4, 6.9 Hz, 1H), 7.27 (d, *J* = 14.1 Hz, 1H), 7.39 (t, *J* = 7.5 Hz, 1H), 7.52 (t, *J* = 6.6 Hz, 1H), 7.65 (d, *J* = 7.5 Hz, 1H), 8.07 (d, *J* = 8.4 Hz, 1H). ¹³C NMR δ 22.3, 29.5, 110.0, 120.1, 121.0, 124.2, 127.8, 130.3, 136.8, 146.1. Anal. Calcd for C₁₁H₁₃N₃: C, 70.56; H, 7.00; N, 22.44. Found: C, 70.73; H, 7.16; N, 23.08.

1-[(E)-1-Butenyl]-1H-1,2,3-benzotriazole (6d). Yellow oil; yield, 50%. ¹H NMR δ 1.01 (t, *J* = 7.5 Hz, 3H), 2.34 (qd, *J* = 7.5, 1.5 Hz, 2H), 6.47 (quintet, *J* = 7.2 Hz, 1H), 7.19–7.32 (m, 2H), 7.40–7.45 (m, 1H), 7.57 (d, *J* = 8.4 Hz, 1H), 7.96–8.00 (m, 1H). ¹³C NMR δ 13.4, 23.3, 110.0, 119.6, 122.3, 124.0, 127.6, 131.1, 132.8, 145.1. Anal. Calcd for C₁₀H₁₁N₃: C, 69.34; H, 6.40; N, 24.26. Found: C, 69.47; H, 6.58; N, 23.87.

Procedure for the preparation of 1,2-dibromo-benzotriazolyl alkanes 7a-d

To a solution of vinylbenzotriazole **6** (5 mmol) in dry dichloromethane was added bromine (0.26 mL, 5 mmol) at 0°C. The mixture was maintained at this temperature for 30 min and then was allowed to warm up to room temperature. The mixture was stirred for 2 h and dichloromethane was evaporated under vacuum to give 1,2-dibromo-benzotriazolyl alkanes **7** in quantitative yield which can be used directly in the next step without further purification.

1-(1,2-Dibromo-2-phenylethyl)-1H-1,2,3-benzotriazole (7a). Light yellow solid; mp 74–75 °C; yield, 100%. ¹H NMR δ 6.21 (d, *J* = 11.4 Hz, 1H), 7.22 (d, *J* = 11.4 Hz, 1H), 7.44–7.53 (m, 4H), 7.60–7.69 (m, 3H), 7.72 (d, *J* = 8.4 Hz, 1H), 8.18 (d, *J* = 8.4 Hz, 1H). ¹³C NMR δ 52.8, 60.9, 110.0, 120.9, 125.1, 128.2, 128.7, 129.2, 129.8, 131.7, 137.5, 146.6.

1-[1,2-Dibromo-2-(3-thienyl)ethyl]-1H-1,2,3-benzotriazole (7b). This compound was obtained as a mixture of isomers. Yellow powder; mp 120–121 °C; yield, 96%. ¹H NMR δ 6.99 (d, *J* = 3.9 Hz, 1H), 7.07 (d, *J* = 3.9 Hz, 1H), 7.10–7.14 (m, 1H), 7.26 (d, *J* = 3.9 Hz, 1H), 7.35 (d, *J* = 3.9 Hz, 1H), 7.47–7.89 (m, 3H), 8.17 (d, *J* = 8.1 Hz, 1H). ¹³C NMR δ 109.8, 109.9, 112.7, 114.1, 114.9, 120.4, 120.5, 120.8, 124.7, 124.8, 125.3, 127.7, 127.8, 127.9, 128.3, 128.5, 130.8, 131.4, 139.9, 146.2.

1-(1,2-Dibromo-3-methylbutyl)-1H-1,2,3-benzotriazole (7c). Light yellow solid; mp 66–67 °C; yield, 100%. ¹H NMR δ 1.10 (d, *J* = 6.3 Hz, 3H), 1.21 (d, *J* = 6.6 Hz, 3H), 2.69 (dh, *J* = 6.3, 2.2 Hz, 1H), 5.27 (dd, *J* = 9.9, 2.1 Hz, 1H), 6.92 (d, *J* = 11.1 Hz, 1H), 7.61 (t, *J* = 7.5 Hz, 1H), 7.32 (t, *J* = 7.5 Hz, 1H), 7.88 (d, *J* = 8.1 Hz, 1H), 8.19 (d, *J* = 8.4 Hz, 1H). ¹³C NMR δ 15.1, 15.9, 22.2, 30.6, 60.3, 62.6, 63.2, 65.1, 103.2, 110.7, 110.8, 119.4, 120.0, 125.9, 126.5, 129.2, 129.5, 131.7, 143.7. Anal. Calcd for C₁₁H₁₃N₃: C, 38.07; H, 3.78; N, 12.11. Found: C, 37.85; H, 3.41; N, 11.74.

1-(1,2-Dibromobutyl)-1H-1,2,3-benzotriazole (7d). Brown oil; yield, 83%. ¹H NMR δ 1.24 (t, *J* = 7.2 Hz, 3H), 2.17 (septet, *J* = 7.2 Hz, 1H), 2.55 (sd, *J* = 7.2, 2.7 Hz, 1H), 5.23 (dt, *J* = 8.1, 2.7 Hz, 1H), 6.89 (d, *J* = 10.4 Hz, 1H), 7.46 (t, *J* = 7.9 Hz, 1H), 7.61 (t, *J* = 8.1 Hz, 2H), 7.70 (d, *J* = 8.3 Hz, 1H), 8.13 (d, *J* = 8.4 Hz, 1H). ¹³C NMR δ 10.5, 29.3, 55.6, 61.0, 110.1, 120.4, 125.0,

128.5, 146.0. Anal. Calcd for $C_{10}H_{11}Br_2N_3$: C, 36.07; H, 3.33; N, 12.62. Found: C, 36.22; H, 3.34; N, 12.31.

Procedure for the preparation of amides 8a-r

To a solution of 1,2-dibromo-benzotriazolyl alkane **7** (1 mmol) dissolved in DMF/H₂O (3 mL/1 mL) was added amine (5 mmol). The mixture was heated at 80 °C for 4 h till the starting material disappeared. Ethyl acetate (30 mL) was added and the diluted mixture was washed with water (3×10 mL) followed by 1M NaOH (10 mL). The organic phase was dried over anhydrous MgSO₄, filtered and concentrated *in vacuo*. The crude product was triturated in ether and filtered to give the desired amide **8**.

N-Phenethyl-2-phenylacetamide (8a). Pale yellow solid; mp 98–100 °C (Lit⁶ mp 94–96 °C); yield, 47%. ¹H NMR δ 2.71 (t, *J* = 6.6 Hz, 2H), 3.44 (q, *J* = 6.9 Hz, 2H), 3.51 (s, 2H), 5.50 (br s, 1H), 7.19 (d, *J* = 6.0 Hz, 2H), 7.15–7.31 (m, 8H). ¹³C NMR δ 35.4, 40.6, 43.7, 126.3, 127.2, 128.5, 128.6, 128.9, 129.3, 134.7, 138.6, 170.8.

N-Butyl-2-phenylacetamide (8b). Yellow solid; mp 43–45 °C (Lit⁷ mp 49–51 °C); yield, 58%. ¹H NMR δ 0.87 (t, *J* = 6.9 Hz, 3H), 1.25 (sextet, *J* = 7.5 Hz, 2H), 1.40 (quintet, *J* = 7.8 Hz, 2H), 3.29 (q, *J* = 6.9 Hz, 2H), 3.55 (s, 2H), 5.66 (br s, 1H), 7.24–7.34 (m, 5H). ¹³C NMR δ 13.6, 19.8, 31.4, 39.3, 43.7, 127.1, 128.8, 129.3, 135.0, 170.9.

2-Phenyl-1-piperidino-1-ethanone (8c). Yellow solid; mp 82–83 °C (Lit⁸ mp 84–86 °C); yield, 61%. ¹H NMR δ 1.31–1.37 (m, 2H), 1.51–1.61 (m, 4H), 3.37 (t, *J* = 5.7 Hz, 2H), 3.58 (t, *J* = 4.8 Hz, 2H), 3.74 (s, 2H), 7.22–7.34 (m, 5H). ¹³C NMR δ 24.3, 25.4, 26.1, 41.1, 42.8, 47.2, 126.6, 128.5, 128.6, 135.3, 169.3.

N,2-Diphenylacetamide (8d). White powder; mp 117 °C (Lit⁶ mp 117–119 °C); yield, 72%. ¹H NMR δ 3.72 (s, 2H), 7.08–7.43 (m, 11H); ¹³C NMR δ 44.8, 119.9, 124.5, 127.6, 128.9, 129.2, 129.5, 134.5, 137.6, 169.3.

N-(tert-Butyl)-2-phenylacetamide (8e). Yellow powder; mp 113–115 °C (Lit⁹ mp 114–115 °C); yield, 68%. ¹H NMR δ 1.28 (s, 9H), 3.48 (s, 2H), 5.20 (br s, 1H), 7.23–7.37 (m, 5H). ¹³C NMR δ 28.6(3C), 44.8, 51.2, 127.1, 128.7, 128.9, 129.2, 129.3, 135.6, 170.4.

2-Phenyl-N-(2-pyridinyl)acetamide (8f). Orange crystals; mp 93–95 °C (Lit¹⁰ mp 124–125 °C); yield, 85%. ¹H NMR δ 3.71 (s, 2H), 6.99 (td, *J* = 7.0, 2.0 Hz, 1H), 7.24–7.33 (m, 5H), 7.66 (td, *J* = 7.0, 2.0 Hz, 1H), 8.20–8.27 (m, 2H), 9.24 (br s, 1H). ¹³C NMR δ 44.3, 114.3, 119.6, 127.2, 128.7, 129.1, 134.0, 138.3, 147.3, 151.5, 169.7. Anal. Calcd for $C_{13}H_{12}N_2O$: C, 73.57; H, 5.70; N, 13.20. Found: C, 73.54; H, 5.80; N, 13.08.

2-Phenyl-N-(2-pyrimidinyl)acetamide (8g). White powder; mp 195 °C (Lit¹¹ mp 193–196 °C); yield, 80%. ¹H NMR δ 4.08 (s, 2H), 6.99 (t, *J* = 4.8 Hz, 1H), 7.27–7.36 (m, 5H), 8.62 (d, *J* = 4.8 Hz, 2H), 9.12 (br s, 1H); ¹³C NMR δ 44.4, 116.4, 127.3, 128.8, 129.6, 134.4, 157.5, 158.4.

N-Phenethyl-2-(2-thienyl)acetamide (8h). Brown oil; yield, 52%; ¹H NMR δ 2.74 (t, *J* = 6.9 Hz, 2H), 3.46 (q, *J* = 6.9 Hz, 3H), 3.72 (s, 2H), 5.76 (br s, 1H), 6.83 (d, *J* = 3.3 Hz, 1H), 6.95 (t, *J* = 5.4 Hz, 1H), 7.08 (d, *J* = 6.6 Hz, 1H), 7.19–7.28 (m, 5H). ¹³C NMR δ 35.4, 37.5, 40.8,

125.6, 126.5, 127.4 (2C), 127.5, 128.7 (2C), 136.0, 138.6, 169.9. HRMS calcd for C₁₄H₁₅NOS: 245.0874, found: 245.0870.

N-Butyl-2-(2-thienyl)acetamide (8i). Brown oil; yield, 92%. ¹H NMR δ 0.89 (t, *J* = 7.3 Hz, 3H), 1.27 (sextet, *J* = 7.0 Hz, 2H), 1.40 (quintet, *J* = 7.2 Hz, 2H), 3.22 (q, *J* = 7.2 Hz, 2H), 3.78 (s, 2H), 5.67 (br s, 1H), 6.93–7.01 (m, 2H), 7.25 (dd, *J* = 5.1, 1.2 Hz, 1H). ¹³C NMR δ 13.7, 19.9, 31.4, 37.5, 39.5, 125.6, 127.3, 127.4 (2C), 136.3, 169.9. HRMS calcd for C₁₀H₁₅NOS: 197.0874, found: 197.0876.

1-Piperidino-2-(2-thienyl)-1-ethanone (8j).³ Brown oil; yield, 88%. ¹H NMR δ 1.38–1.54 (m, 6H), 3.37 (t, *J* = 5.8 Hz, 2H), 3.50 (t, *J* = 5.8 Hz, 2H), 3.84 (s, 2H), 6.82–6.88 (m, 2H), 7.12 (dd, *J* = 5.1, 1.2 Hz, 1H). ¹³C NMR δ 24.3, 25.3, 26.1, 35.1, 43.0, 47.4, 124.5, 125.8, 126.7, 136.7, 168.3.

1-Methyl-1-piperidin-1-yl-propan-1-one (8k).¹² Yellow oil; yield, 50%. ¹H NMR δ 0.97 (d, *J* = 6.6 Hz, 6H), 1.23 (d, *J* = 6.6 Hz, 1H), 1.52–1.56 (m, 6H), 2.20 (d, *J* = 6.6 Hz, 2H), 3.41 (m, 2H), 3.56 (m, 2H). ¹³C NMR δ 17.9, 22.6, 24.4, 25.5, 25.7, 26.5, 42.0, 42.4, 46.8, 109.1, 119.9, 123.9, 127.7, 170.7.

N-Butylbutanamide (8l).¹³ Colorless oil; yield, 82%. ¹H NMR δ 0.88 (t, *J* = 7.2 Hz, 3H), 0.91 (t, *J* = 7.5 Hz, 3H), 1.30 (sextet, *J* = 7.0 Hz, 2H), 1.46 (quintet, *J* = 7.0 Hz, 2H), 1.62 (sextet, *J* = 7.0 Hz, 2H), 2.15 (t, *J* = 7.3 Hz, 2H), 3.20 (q, *J* = 6.9 Hz, 2H), 6.54 (br s, 1H). ¹³C NMR δ 13.5 (2C), 19.1, 19.9, 31.4, 38.3, 39.1, 173.4. Anal. Calcd for C₈H₁₇N₁O: C, 67.09; H, 11.96; N, 9.78. Found: C, 66.82; H, 12.46; N, 9.65.

N-[2-(Dimethylamino)ethyl]butanamide (8m).¹⁴ Colorless oil; yield, 32%. ¹H NMR δ 0.87 (t, *J* = 7.2 Hz, 3H), 1.58–1.62 (m, 4H), 2.07 (t, *J* = 7.8 Hz, 2H), 2.17 (s, 6H), 2.31 (t, *J* = 7.8 Hz, 2H), 3.21–3.27 (m, 2H), 3.69 (br s, 1H). ¹³C NMR δ 13.6, 18.9, 26.0, 38.5, 38.6, 45.0, 58.0, 173.0.

1-Morpholino-1-butanone (8n).¹⁵ Colorless oil; yield, 50%. ¹H NMR δ 0.97 (t, *J* = 7.5 Hz, 3H), 1.66 (sextet, *J* = 7.4 Hz, 2H), 2.31 (t, *J* = 7.5 Hz, 2H), 3.47–3.50 (m, 2H), 3.62–3.69 (m, 6H). ¹³C NMR δ 13.7, 18.5, 34.7, 41.5, 45.7, 66.4, 66.6, 171.3.

1-(4-Methylpiperazino)-1-butanone (8o).¹⁶ Colorless oil; yield, 62%. ¹H NMR 0.97 (t, *J* = 7.3 Hz, 3H), 1.65 (sextet, *J* = 7.5 Hz, 2H), 2.31 (s, 3H), 2.31 (t, *J* = 7.5 Hz, 2H), 2.39 (quintet, *J* = 5.1 Hz, 2H), 3.50 (t, *J* = 4.8 Hz, 2H), 3.63 (t, *J* = 4.8 Hz, 2H). ¹³C NMR δ 13.4, 18.2, 34.6, 40.7, 45.4, 54.2, 54.6, 170.9. Anal. Calcd for C₉H₁₈N₂: C, 63.49; H, 10.66; N, 16.45. Found: C, 62.56; H, 10.97; N, 16.19.

N-Phenylbutanamide (8p). White powder; mp 82–84 °C (Lit¹⁷ mp 92 °C); yield, 95%. ¹H NMR δ 0.98 (t, *J* = 7.2 Hz, 3H), 1.74 (quintet, *J* = 7.4 Hz, 2H), 2.32 (t, *J* = 7.4 Hz, 2H), 7.08 (t, *J* = 7.4 Hz, 1H), 7.29 (t, *J* = 7.8 Hz, 2H), 7.53 (d, *J* = 7.8 Hz, 2H), 7.70 (br s, 1H). ¹³C NMR δ 13.8, 19.1, 39.6, 119.9, 124.2, 128.9, 138.1, 171.7. Anal. Calcd for C₁₀H₁₃N₁O: C, 73.59; H, 8.03; N, 8.58. Found: C, 73.49; H, 8.31; N, 8.60.

N-(4-Pyridinyl)butanamide (8q). White powder; mp 136–138 °C; yield, 95%. ¹H NMR δ 0.99 (t, *J* = 7.3 Hz, 3H), 1.75 (sextet, *J* = 7.4 Hz, 2H), 2.38 (t, *J* = 7.2 Hz, 2H), 7.54 (d, *J* = 6.3 Hz,

2H), 8.46 (d, $J = 6.3$ Hz, 2H), 8.58 (br s, 1H). ^{13}C NMR δ 13.6, 18.7, 39.5, 113.6, 145.6, 150.3, 172.5. Anal. Calcd for $\text{C}_9\text{H}_{12}\text{N}_2$: C, 65.83; H, 7.37; N, 17.06. Found: C, 65.45; H, 7.66; N, 15.97. ***N*-(1-Naphthyl)butanamide (8r)**. Violet powder; mp 113–115 °C (Lit¹⁸ mp 120 °C); yield, 68%. ^1H NMR δ 1.05 (t, $J = 7.3$ Hz, 3H), 1.82 (quintet, $J = 7.3$ Hz, 2H), 2.45 (t, $J = 7.3$ Hz, 2H), 7.43 (t, $J = 8.1$ Hz, 1H), 7.46–7.50 (m, 2H), 7.64 (br s, 1H), 7.67 (d, $J = 8.2$ Hz, 1H), 7.81–7.87 (m, 3H). ^{13}C NMR δ 13.6, 19.1, 38.8, 121.3, 121.7, 125.3, 125.7, 125.8, 127.7, 128.2, 132.4, 133.9, 172.5. Anal. Calcd for $\text{C}_{14}\text{H}_{15}\text{N}_1\text{O}$: C, 78.84; H, 7.09; N, 6.57. Found: C, 78.80; H, 7.24; N, 6.63.

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